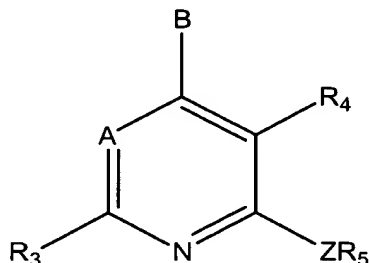


In the Claims

Please amend claims 1, 2, 12, 14, 15, 29, 32, 36, 39 and 40:

Claim 1 (Twice Amended). A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

A is $-\text{CR}_7$;

B is $-\text{NR}_1\text{R}_2$, $-\text{CR}_1\text{R}_2\text{R}_{11}$, $-\text{C}(=\text{CR}_2\text{R}_{12})\text{R}_1$, $-\text{NHCHR}_1\text{R}_2$, $-\text{OCHR}_1\text{R}_2$, $-\text{SCHR}_1\text{R}_2$, $-\text{CHR}_2\text{OR}_1$, $-\text{CHR}_1\text{OR}_2$, $-\text{CHR}_2\text{SR}_1$, $-\text{C}(\text{S})\text{R}_2$, $-\text{C}(\text{O})\text{R}_2$, $-\text{CHR}_2\text{NR}_1\text{R}_2$, $-\text{CHR}_1\text{NHR}_2$, $-\text{CHR}_1\text{N}(\text{CH}_3)\text{R}_2$, or $-\text{NR}_{12}\text{NR}_1\text{R}_2$;

B¹
Z is NH, O, S, $-\text{N}(\text{C}_1\text{-C}_2 \text{ alkyl})-$, $-\text{N}(\text{C}(\text{O})\text{CF}_3)-$, or $-\text{C}(\text{R}_{13}\text{R}_{14})-$, wherein R_{13} and R_{14} are each, independently, hydrogen, trifluoromethyl or methyl, or one of R_{13} and R_{14} is cyano and the other is hydrogen or methyl, or $-\text{C}(\text{R}_{13}\text{R}_{14})$ is a cyclopropyl group, or Z is nitrogen or CH and forms a five or six membered heterocyclic ring fused with R_5 , which ring optionally comprises two or three further hetero members selected independently from oxygen, nitrogen, NR_{12} , and $\text{S}(\text{O})_m$, and optionally comprises from one to three double bonds, and is optionally substituted with halo, $\text{C}_1\text{-C}_4$ alkyl, $-\text{O}(\text{C}_1\text{-C}_4 \text{ alkyl})$, NH_2 , NHCH_3 , $\text{N}(\text{CH}_3)_2$, CF_3 , or OCF_3 , with the proviso that said ring does not contain any $-\text{S-S}-$, $-\text{S-O}-$, $-\text{N-S}-$, or $-\text{O-O}-$ bonds, and does not comprise more than two oxygen or $\text{S}(\text{O})_m$ heterologous members;

R_1 is $\text{C}(\text{O})\text{H}$, $\text{C}(\text{O})(\text{C}_1\text{-C}_6 \text{ hydrocarbyl})$, $\text{C}(\text{O})(\text{C}_1\text{-C}_6 \text{ hydrocarbylene})(\text{C}_3\text{-C}_8 \text{ cyclohydrocarbyl})$, $\text{C}(\text{O})(\text{C}_3\text{-C}_8 \text{ cyclohydrocarbylene})(\text{C}_3\text{-C}_8 \text{ cyclohydrocarbyl})$, $\text{C}(\text{O})(\text{C}_1\text{-C}_6 \text{ hydrocarbylene})(\text{C}_4\text{-C}_8 \text{ heterocyclohydrocarbyl})$, $-\text{C}(\text{O})(\text{C}_3\text{-C}_8 \text{ cyclohydrocarbylene})(\text{C}_4\text{-C}_8 \text{ heterocyclohydrocarbyl})$, $\text{C}_1\text{-C}_6 \text{ hydrocarbyl}$, $\text{C}_3\text{-C}_8 \text{ cyclohydrocarbyl}$, $\text{C}_4\text{-C}_8 \text{ heterocyclohydrocarbyl}$, $-(\text{C}_1\text{-C}_6 \text{ hydrocarbylene})(\text{C}_3\text{-C}_8 \text{ cyclohydrocarbyl})$, $\text{C}_3\text{-C}_8 \text{ cyclohydrocarbylene})(\text{C}_3\text{-C}_8 \text{ cyclohydrocarbyl})$, $-(\text{C}_1\text{-C}_6 \text{ hydrocarbylene})(\text{C}_4\text{-C}_8 \text{ heterocyclohydrocarbyl})$, $-(\text{C}_3\text{-C}_8 \text{ cyclohydrocarbylene})(\text{C}_4\text{-C}_8 \text{ heterocyclohydrocarbyl})$, or $-\text{O-aryl}$, or $-\text{O}(\text{C}_1\text{-C}_6 \text{ hydrocarbylene})\text{-aryl}$; wherein said aryl,

β
 C_4-C_8 heterocyclohydrocarbyl, C_1-C_6 hydrocarbyl, C_3-C_8 cyclohydrocarbyl, C_3-C_8 cyclohydrocarbylene, and C_1-C_6 hydrocarbylene groups may each independently be optionally substituted with from one to six fluoro and may each independently be optionally substituted with one or two substituents R_8 independently selected from the group consisting of C_1-C_4 hydrocarbyl, $-C_3-C_8$ cyclohydrocarbyl, hydroxy, chloro, bromo, iodo, CF_3 , $-O-(C_1-C_6$ hydrocarbyl), $-O-(C_3-C_8$ cyclohydrocarbyl), $-O-CO-(C_1-C_4$ hydrocarbyl), $-O-CO-NH(C_1-C_4$ hydrocarbyl), $-O-CO-N(R_{24})(R_{25})$, $-N(R_{24})(R_{25})$, $-S(C_1-C_4$ hydrocarbyl), $-S(C_3-C_8$ cyclohydrocarbyl), $-N(C_1-C_4$ hydrocarbyl) $CO(C_1-C_4$ hydrocarbyl), $-NHCO(C_1-C_4$ hydrocarbyl), $-COO(C_1-C_4$ hydrocarbyl), $-CONH(C_1-C_4$ hydrocarbyl), $-CONC_1-C_4$ hydrocarbyl), $(C_1-C_2$ hydrocarbyl), CN , NO_2 , $-OSO_2(C_1-C_4$ hydrocarbyl), $S^+(C_1-C_6$ hydrocarbyl)(C_1-C_2 hydrocarbyl), $-SO(C_1-C_4$ hydrocarbyl) and $-SO_2(C_1-C_4$ hydrocarbyl); and wherein the C_1-C_6 hydrocarbyl, C_1-C_6 hydrocarbylene, C_3-C_8 cyclohydrocarbyl, C_3-C_8 cyclohydrocarbylene, and C_5-C_8 heterocyclohydrocarbyl moieties of R_1 may optionally independently contain from one to three double or triple bonds; and wherein the C_1-C_4 hydrocarbyl moieties and C_1-C_6 hydrocarbyl moieties of R_8 can optionally independently be substituted with hydroxy, amino, C_1-C_4 alkyl, aryl, $-CH_2$ -aryl, C_3-C_5 cycloalkyl, or $-O-(C_1-C_4$ alkyl), and can optionally independently be substituted with from one to six fluoro, and can optionally contain one or two double or triple bonds; and wherein each heterocyclohydrocarbyl group of R_1 contains from one to three heteromoieties selected from oxygen, $S(O)_m$, nitrogen, and NR_{12} ;

R_2 is hydrogen, C_1-C_{12} hydrocarbyl, C_3-C_8 cyclohydrocarbyl, C_4-C_8 heterocyclohydrocarbyl, $-(C_1-C_6$ hydrocarbylene)(C_3-C_8 cyclohydrocarbyl), $-(C_3-C_8$ cyclohydrocarbylene)(C_3-C_8 cyclohydrocarbyl), $-(C_1-C_6$ hydrocarbylene)(C_4-C_8 heterocyclohydrocarbyl), $-(C_3-C_6$ cyclohydrocarbylene)(C_4-C_8 heterocyclohydrocarbyl), aryl, $-(C_1-C_6$ hydrocarbylene)aryl, or $-(C_3-C_8$ cyclohydrocarbylene)(aryl); wherein each of the foregoing R_2 groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, and C_1-C_6 alkyl, wherein one of said one to three substituents can further be selected from bromo, iodo, C_1-C_6 alkoxy, $-OH$, $-O-CO-(C_1-C_6$ alkyl), $-O-CO-N(C_1-C_4$ alkyl)(C_1-C_2 alkyl), $-S(C_1-C_6$ alkyl), $-S(O)(C_1-C_6$ alkyl), $-S(O)_2(C_1-C_6$ alkyl), $S^+(C_1-C_6$ alkyl)(C_1-C_2 alkyl), I , CN , and NO_2 ; and wherein the C_1-C_{12} hydrocarbyl, $-(C_1-C_6$ hydrocarbylene), and cyclohydrocarbyl groups of 5 - 8 carbon atoms, cyclohydrocarbylene groups of 5 to 8 carbon atoms and heterocyclohydrocarbyl groups of 5 to 8 atoms of R_2 may optionally independently contain from one to three double or triple

bonds; and wherein each heterocyclohydrocarbonyl group of R_2 contains from one to three heteromoieties selected from oxygen, $S(O)_m$, nitrogen, and NR_{12} ;

or when R_1 and R_2 are as in $-NHCHR_1R_2$, $-OCHR_1R_2$, $-SCHR_1R_2$, $-CHR_1R_2$ or $-NR_1R_2$, R_1 and R_2 of B may form a saturated 5- to 8-membered ring which may optionally contain one or

two double bonds and in which one or two of the ring carbons may optionally be replaced by an

oxygen, $S(O)_m$, nitrogen or NR_{12} ; and which carbocyclic ring can optionally be substituted with

from 1 to 3 substituents selected from the group consisting of hydroxy, C_1 - C_4 alkyl, fluoro, chloro, bromo, iodo, CF_3 , $-O-(C_1-C_4 \text{ alkyl})$, $-O-CO-(C_1-C_4 \text{ alkyl})$, $-O-CO-NH(C_1-C_4 \text{ alkyl})$, $-O-CO-N(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$, $-NH(C_1-C_4 \text{ alkyl})$, $-N(C_1-C_2 \text{ alkyl})(C_1-C_4 \text{ alkyl})$, $-S(C_1-C_4 \text{ alkyl})$, $-N(C_1-C_4 \text{ alkyl})CO(C_1-C_4 \text{ alkyl})$, $-NHCO(C_1-C_4 \text{ alkyl})$, $-COO(C_1-C_4 \text{ alkyl})$, $-CONH(C_1-C_4 \text{ alkyl})$, $-CON(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$, CN , NO_2 , $-OSO_2(C_1-C_4 \text{ alkyl})$, $-SO(C_1-C_4 \text{ alkyl})$, and $-SO(C_1-C_4 \text{ alkyl})$, wherein one of said one to three substituents can further be selected from phenyl;

R_3 is methyl, ethyl, fluoro, chloro, bromo, iodo, cyano, methoxy, OCF_3 , NH_2 , $NH(C_1-C_2 \text{ alkyl})$, $N(CH_3)_2$, $-NHCOCF_3$, $-NHCH_2CF_3$, $S(O)_m(C_1-C_4 \text{ alkyl})$, $CONH_2$, $-CONHCH_3$, $CON(CH_3)_2$, $-CF_3$, or CH_2OCH_3 ;

R_4 is hydrogen, C_1 - C_4 hydrocarbonyl, C_3 - C_5 cycloalkyl, $-(C_1-C_4 \text{ hydrocarbonylene})(C_3-C_5 \text{ cycloalkyl})$, $-(C_3-C_5 \text{ cycloalkylene})(C_3-C_6 \text{ cycloalkyl})$, cyano, fluoro, chloro, bromo, iodo, $-OR_{24}$ C_1 - C_6 alkoxy, $-O-$ cycloalkyl, $-O-(C_1-C_4 \text{ hydrocarbonylene})(C_3-C_5 \text{ cycloalkyl})$, $-O-(C_3-C_5 \text{ cycloalkylene})(C_3-C_5 \text{ cycloalkyl})$, $-CH_2SC(S)O(C_1-C_4 \text{ alkyl})$, CH_2OCF_3 , CF_3 , amino, nitro, $-NR_{24}R_{25}$, $-(C_1-C_4 \text{ hydrocarbonylene})-OR_{24}$, $-(C_1-C_4 \text{ hydrocarbonylene})Cl$, $-(C_1-C_4 \text{ hydrocarbonylene})NR_{24}R_{25}$, $-NHCOR_{24}$, $-NHCONR_{24}R_{25}$, $-CH=NOR_{24}$, $-NHNr_{24}R_{25}$, $-S(O)_mR_{24}$, $-C(O)R_{24}$, $-OC(O)R_{24}$, $-C(O)CN$, $-C(O)NR_{24}R_{25}$, $-C(O)NHNr_{24}R_{25}$, and $-COOR_{24}$, wherein the hydrocarbonyl and hydrocarbonylene groups of R_4 may optionally independently contain one or two double or triple bonds and may optionally independently be substituted with one or two substituents R_{10} independently selected from hydroxy, amino, $-NHCOCH_3$, $-NHCOCH_2Cl$, $-NH(C_1-C_2 \text{ alkyl})$, $-N(C_1-C_2 \text{ alkyl})(C_1-C_2 \text{ alkyl})$, $-COO(C_1-C_4 \text{ alkyl})$, $-COOH$, $-CO(C_1-C_4 \text{ alkyl})$, C_1 - C_6 alkoxy, C_1 - C_3 thioalkyl, cyano and nitro, and with one to four substituents independently selected from fluoro and chloro;

R_5 is aryl or heteroaryl and is substituted with from one to four substituents R_{27} independently selected from halo, C_1 - C_{10} hydrocarbonyl, $-(C_1-C_4 \text{ hydrocarbonylene})(C_3-C_8$

cycloalkyl), $-(C_1-C_4 \text{ hydrocarbylene})(C_4-C_8 \text{ heterocycloalkyl})$, $-(C_3-C_8 \text{ cycloalkyl})$, $-(C_4-C_8 \text{ heterocycloalkyl})$, $-(C_3-C_8 \text{ cycloalkylene})(C_3-C_8 \text{ cycloalkyl})$, $-(C_3-C_8 \text{ cycloalkylene})(C_4-C_8 \text{ heterocycloalkyl})$, $C_1-C_4 \text{ haloalkyl}$, $C_1-C_4 \text{ haloalkoxy}$, nitro, cyano, $-NR_{24}R_{25}$, $-NR_{24}COR_{25}$, $-NR_{24}CO_2R_{26}$, $-COR_{24}$, $-OR_{25}$, $-CONR_{24}R_{25}$, $-CON(OR_{22})R_{23}$, $-CO_2R_{26}$, $-C=N(OR_{22})R_{23}$, and $-S(O)_mR_{23}$; wherein said C_1-C_{10} alkyl, C_3-C_8 cycloalkyl, $(C_1-C_4 \text{ hydrocarbylene})$, $(C_3-C_8 \text{ cycloalkyl})$, $(C_3-C_8 \text{ cycloalkylene})$, and $(C_4-C_8 \text{ heterocycloalkyl})$ groups can be optionally substituted with from one to three substituents independently selected from C_1-C_4 alkyl, C_3-C_8 cycloalkyl, $(C_1-C_4 \text{ hydrocarbylene})(C_3-C_8 \text{ cycloalkyl})$, $-(C_3-C_8 \text{ cycloalkylene})(C_3-C_8 \text{ cycloalkyl})$, C_1-C_4 haloalkyl, hydroxy, C_1-C_6 alkoxy, nitro, halo, cyano, $-NR_{24}R_{25}$, $-NR_{24}COR_{25}$, $NR_{24}CO_2R_{26}$, $-COR_{24}$, $-OR_{25}$, $-CONR_{24}R_{25}$, CO_2R_{26} , $-CO(NOR_{22})R_{25}$, and $-S(O)_mR_{23}$; and wherein two adjacent substituents of the R_5 group can optionally form a 5-7 membered ring, saturated or unsaturated, fused to R_5 , which ring optionally can contain one, two, or three heterologous members independently selected from O, $S(O)_m$, and N, but not any $-S-S-$, $-O-O-$, $-S-O-$, or $-N-S-$ bonds, and which ring is optionally substituted with C_1-C_4 alkyl, C_3-C_8 cycloalkyl, $-(C_1-C_4 \text{ alkylene})(C_3-C_8 \text{ cycloalkyl})$, $-(C_3-C_8 \text{ cycloalkylene})(C_3-C_8 \text{ cycloalkyl})$, C_1-C_4 haloalkyl, nitro, halo, cyano, $-NR_{24}R_{25}$, $NR_{24}COR_{25}$, $NR_{24}CO_2R_{26}$, $-COR_{24}$, $-OR_{25}$, $-CONR_{24}R_{25}$, CO_2R_{26} , $-CO(NOR_{26})R_{25}$, or $-S(O)_mR_{23}$; wherein one of said one to four optional substituents R_{27} , can further be selected from $-SO_2NH(C_1-C_4 \text{ alkyl})$, $-SO_2NH(C_1-C_4 \text{ alkylene})(C_3-C_8 \text{ cycloalkyl})$, $SO_2NH(C_3-C_8 \text{ cycloalkyl})$, $-SO_2NH(C_3-C_8 \text{ cycloalkylene})(C_3-C_8 \text{ cycloalkyl})$, $-SO_2N(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$, $-SO_2NH_2$, $-NHSO_2(C_1-C_4 \text{ alkyl})$, $-NHSO_2(C_3-C_8 \text{ cycloalkyl})$, $-NHSO_2(C_1-C_4 \text{ alkylene})(C_3-C_8 \text{ cycloalkyl})$, and $-NHSO_2(C_3-C_8 \text{ cycloalkylene})(C_3-C_8 \text{ cycloalkyl})$; and wherein the hydrocarbyl, and hydrocarbylene groups of R_5 may independently optionally contain one double or triple bond;

R_6 is hydrogen, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, $-(C_1-C_6 \text{ alkylene})(C_3-C_8 \text{ cycloalkyl})$, or $-(C_3-C_8 \text{ cycloalkylene})(C_3-C_8 \text{ cycloalkyl})$, wherein said alkyl and cycloalkyl may optionally be substituted with one hydroxy, methoxy, ethoxy or fluoro group;

or R_6 and R_4 can together form an oxo ($=O$) group, or can be connected to form a 3-8 membered carbocyclic ring, optionally containing one to three double bonds, and optionally containing one, two, or three heterologous ring members selected from O, SO_m , N, and NR_{12} , but not containing any $-O-O-$, $-S-O-$, $-S-S-$, or $-N-S-$ bonds, and further optionally substituted with C_1-C_4 hydrocarbyl or C_3-C_6 cycloalkyl, wherein said C_1-C_4 hydrocarbyl substituent may optionally contain one double or triple bond;

R_7 is hydrogen, methyl, fluoro, chloro, bromo, iodo, cyano, hydroxy, $-O(C_1-C_2 \text{ alkyl})$, $-O(\text{cyclopropyl})$, $-COO(C_1-C_2 \text{ alkyl})$, $-COO(C_3-C_8 \text{ cycloalkyl})$, $-OCF_3$, $-CF_3$, $-CH_2OH$ or CH_2OCH_3 ;

R₁₁ is hydrogen, hydroxy, fluoro, ethoxy, or methoxy;

R₁₂ is hydrogen or C₁-C₄ alkyl;

R₂₂ is independently at each occurrence selected from hydrogen, C₁-C₁₄ alkyl, C₁-C₁₄ haloalkyl, C₃-C₆ alkenyl, C₃-C₆ alkynyl, C₃-C₈ cycloalkyl, (C₃-C₈ cycloalkylene)(C₃-C₈ cycloalkyl), and (C₁-C₄) alkylene)(C₃-C₈ cycloalkyl);

R₂₃ is independently at each occurrence selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₂-C₈ alkoxyalkyl, C₃-C₈ cycloalkyl, -(C₁-C₄ alkylene)(C₃-C₈ cycloalkyl), -(C₃-C₈ cycloalkylene)(C₃-C₈ cycloalkyl), aryl, -(C₁-C₄ alkylene)aryl, piperidine, pyrrolidine, piperazine, N-methylpiperazine, morpholine, and thiomorpholine;

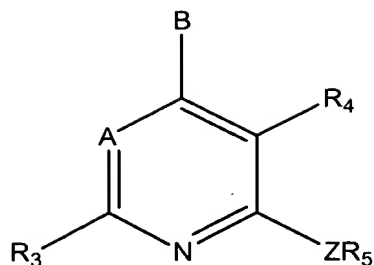
B
R₂₄ and R₂₅ are independently at each occurrence selected from hydrogen, -C₁-C₄ alkyl, C₁-C₄ haloalkyl, -(C₁-C₄ alkylene)OH, -(C₁-C₄ alkylene)-O-(C₁-C₄ alkyl), -(C₁-C₄ alkylene)-O-(C₃-C₅ cycloalkyl), C₃-C₈ cycloalkyl, -(C₁-C₄ alkylene)(C₃-C₈ cycloalkyl), -(C₃-C₈ cycloalkylene)(C₃-C₈ cycloalkyl), -C₄-C₈ heterocyclohydrocarbyl, -(C₁-C₄ alkylene)(C₄-C₈ heterocyclohydrocarbyl), -(C₃-C₈ cycloalkylene)(C₄-C₈ heterocyclohydrocarbyl), aryl, and -(C₁-C₄ alkylene)(aryl), wherein the -C₄-C₈ heterocyclohydrocarbyl groups can each independently optionally be substituted with aryl, CH₂-aryl, or C₁-C₄ alkyl, and can optionally contain one or two double or triple bonds; or, when R₂₄ and R₂₅ are as NR₂₄R₂₅, -C(O)NR₂₄R₂₅, -(C₁-C₄ alkylene)NR₂₄R₂₅, or -NHCONR₂₄R₂₅, then NR₂₄R₂₅ may further optionally form a 4 to 8 membered heterocyclic ring optionally containing one or two further hetero members independently selected from S(O)_m, oxygen, nitrogen, and NR₁₂, and optionally containing from one to three double bonds;

R₂₆ is independently at each occurrence selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₃-C₈ cycloalkyl, -(C₁-C₄ alkylene)(C₃-C₈ cycloalkyl), -(C₃-C₈ cycloalkylene)(C₃-C₈ cycloalkyl), aryl, and -(C₁-C₄ alkylene)(aryl); and

wherein each m is independently zero, one, or two,

with the proviso that heterocyclohydrocarbylene groups of the compound of formula I, do not comprise any -S-S-, -S-O-, -N-S-, or -O-O- bonds, and do not comprise more than two oxygen or S(O)_m heterologous members.

Claim 2 (Twice Amended). A compound according to claim 1 of the formula



or a pharmaceutically acceptable salt thereof, wherein

A is CR₇;

B is -NR₁R₂, -CR₁R₂R₁₁, -C(=CR₂R₁₂)R₁, -NHCHR₁R₂, -OCHR₁R₂, -SCHR₁R₂, -CHR₂OR₁₂, -CHR₂SR₁₂, -C(S)R₂ or -C(O)R₂;

Z is -NH, O, S, N(C₁-C₂ alkyl) or C(R₁₃R₁₄) wherein R₁₃ and R₁₄ are each independently, hydrogen, trifluoromethyl or methyl or one of R₁₃ and R₁₄ is cyano and the other is hydrogen or methyl;

R₁ is C₁-C₆ hydrocarbyl which may optionally be substituted with one or two substituents R₈ independently selected from the group consisting of hydroxy, fluoro, chloro, bromo, iodo, CF₃, C₁-C₄ alkoxy, -O-CO-(C₁-C₄ hydrocarbyl), -O-CO-NH(C₁-C₄ hydrocarbyl), -O-CO-N(C₁-C₄ hydrocarbyl)(C₁-C₂ hydrocarbyl), -NH(C₁-C₄ hydrocarbyl), -N(C₁-C₂ alkyl)(C₁-C₄ hydrocarbyl), -S(C₁-C₄ alkyl), -N(C₁-C₄)CO(C₁-C₄ hydrocarbyl), -NHCO(C₁-C₄ hydrocarbyl), -COO(C₁-C₄ hydrocarbyl)hydrocarbyl, -CONH(C₁-C₄ hydrocarbyl), -CON(C₁-C₄ hydrocarbyl)(C₁-C₂ alkyl), CN, NO₂, -SO(C₁-C₄ hydrocarbyl) and -SO₂(C₁-C₄ hydrocarbyl), and wherein said C₁-C₆ hydrocarbyl and the (C₁-C₄)hydrocarbyl moieties in the foregoing R₁ groups may optionally contain one carbon-carbon double or triple bond;

R₂ is C₁-C₁₂ hydrocarbyl, aryl or -(C₁-C₄ hydrocarbylene)aryl wherein said aryl is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, benzisothiazolyl, benzisoxazolyl, benzimidazolyl, indolyl, or benzoxazolyl; 3- to 8-membered cycloalkyl or -(C₁-C₆ alkylene)cycloalkyl, wherein one or two of the ring carbons of said cycloalkyl having at least 4 ring members and the cycloalkyl moiety of said -(C₁-C₆ alkylene)cycloalkyl having at least 4 ring members may optionally be replaced by an oxygen or sulfur atom or by N-R₉ wherein R₉ is hydrogen or C₁-C₄ alkyl; and wherein each of the foregoing R₂ groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro and C₁-C₄ alkyl, or with one substituent selected from bromo, iodo, C₁-C₆ alkoxy, -O-CO-(C₁-C₆ alkyl), -O-CO-N(C₁-C₄ alkyl)(C₁-C₂ alkyl), -S(C₁-C₆ alkyl), CN, NO₂,

-SO(C₁-C₄ alkyl), and -SO₂(C₁-C₄ alkyl), and wherein said C₁-C₁₂ hydrocarbyland the C₁-C₄ hydrocarboylene moiety of said -(C₁-C₄ hydrocarbylene)aryl may optionally contain one carbon-carbon double or triple bond;

or -NR₁R₂ or -CR₁R₂R₁₁ may form a saturated 5- to 8-membered carbocyclic ring which may optionally contain one or two carbon-carbon double bonds and in which one or two of the ring carbons may optionally be replaced by an oxygen or sulfur atom;

R₃ is methyl, ethyl, fluoro, chloro, bromo, iodo, cyano, methoxy, OCF₃, methylthio, methylsulfonyl, CH₂OH, or CH₂OCH₃;

R₄ is hydrogen, C₁-C₄ hydrocarbyl, fluoro, chloro, bromo, iodo, C₁-C₄ alkoxy, trifluoromethoxy, -CH₂OCH₃, -CH₂OCH₂CH₃, -CH₂CH₂OCH₃, -CH₂OF₃, CF₃, amino, nitro, -NH(C₁-C₄ alkyl), -N(CH₃)₂, -NHCOCH₃, -NHCONHCH₃, -SO_n(C₁-C₄ hydrocarbyl) wherein n is 0, 1 or 2, cyano, hydroxy, -CO(C₁-C₄ hydrocarbyl), -CHO, cyano or -COO(C₁-C₄ alkyl) wherein said C₁-C₄ hydrocarbyl may optionally contain one double or triple bond and may optionally be substituted with one substituent selected from hydroxy, amino, -NHCOCH₃, -NH(C₁-C₂ alkyl), -N(C₁-C₂ alkyl)₂, -COO(C₁-C₄ alkyl), -CO(C₁-C₄ alkyl), C₁-C₃ alkoxy, C₁-C₃ thioalkyl, fluoro, chloro, cyano and nitro;

R₅ is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, furanyl, benzofuranyl, benzothiazolyl, or indolyl, wherein each of the above groups R₅ is substituted with from one to three substituents independently selected from fluoro, chloro, C₁-C₆ alkyl, and C₁-C₆ alkoxy, or with one substituent selected from hydroxy, iodo, bromo, formyl, cyano, nitro, trifluoromethyl, amino, -(C₁-C₆ alkyl)O(C₁-C₆)alkyl, -NHCH₃, -N(CH₃)₂, -COOH, -COO(C₁-C₄ alkyl), -CO(C₁-C₄ alkyl), -SO₂NH(C₁-C₄ alkyl), -SO₂N(C₁-C₄ alkyl)(C₁-C₂ alkyl), -SO₂NH₂, -NHSO₂(C₁-C₄ alkyl), -S(C₁-C₆ alkyl) and -SO₂(C₁-C₆ alkyl), and wherein the C₁-C₄ alkyl and C₁-C₆ alkyl moieties of the foregoing R₅ groups may optionally be substituted with one or two fluoro groups or with one substituent selected from hydroxy, amino, methylamino, dimethylamino and acetyl;

R₁₁ is hydrogen, hydroxy, fluoro, or methoxy;

R₁₂ is hydrogen or C₁-C₄ alkyl; and

or a pharmaceutically acceptable salt of such compound.

Claim 12 (Amended). A compound according to claim 1, wherein said compound is selected from the group consisting of:

[3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl]-diethyl-amine;

[3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl]-ethyl-propyl-amine;

butyl-[3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl]-ethyl-amine;

4-(1-ethyl-propoxy)-3,6-dimethyl-2-(2,4,6-trimethyl-phenylsulfanyl)-pyridine;
butyl-[2-(4-chloro-2,6-dimethyl-phenoxy)-3,6-dimethyl-pyridin-4-yl]-ethyl-amine;
[3,6-dimethyl-[2-(2,4,6-trimethyl-phenylsulfanyl)-pyridin-4-yl]-ethyl-propyl-amine;
[2-(4-chloro-2,6-dimethyl-phenoxy)-3,6-dimethyl-pyridin-4-yl]-ethyl-propyl-amine;
N4-(1-ethyl-propyl)-6-methyl-3-nitro-N2-(2,4,6-trimethyl-phenyl)-pyridine-2,4-diamine;
3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl]-ethyl-(2,2,2-trifluoro-ethyl)-amine;
N4-(1-ethyl-propyl)-6-methyl-N2-(2,4,6-trimethyl-phenyl)-pyridine-2,3,4-triamine;
(N-(1-ethyl-propyl)-2-methyl-5-nitro-N'-(2,4,6-trimethyl-pyridin-3-yl)-pyrimidine-4,6-
diamine;
[2-(4-chloro-2,6-dimethyl-phenoxy)-3,6-dimethyl-pyridin-4-yl]-diethyl-amine;
(1-ethyl-propyl)-[5-methyl-3-(2,4,6-trimethyl-phenyl)-3H-imidazo [4,5-b]pyridin-7-yl-
amine;
[2,5-dimethyl-3-(2,4,6-trimethyl-phenyl)-3H-imidazo[4,5-b]pyridin-4-yl]-(1-ethyl-propyl)-
amine;
[4-(1-ethyl-propoxy)-3,6-dimethyl-pyridin-2-yl]-(2,4,6-trimethylphenyl)-amine;
[4-(1-ethyl-propoxy)-3,6-dimethyl-2-(2,4,6-trimethylphenoxy)-pyridine;
[3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl]-(1-ethyl-propyl)-amine; and
[2-(4-chloro-2,6-dimethyl-phenoxy)-3,6-dimethyl-pyridin-4-yl]-(1-ethyl-propyl)-amine
or pharmaceutically acceptable salt of one of the above compounds.

B²

Claim 13 (Twice Amended). A pharmaceutical composition for the treatment of
(a) a disorder or condition the treatment of which can be effected or facilitated by
antagonizing CRF or (b) a disorder or condition selected from inflammatory disorders, pain,
asthma, psoriasis and allergies; generalized anxiety disorder; panic; phobias;
obsessive-compulsive disorder; post-traumatic stress disorder; sleep disorders induced by
stress; pain perception; mood disorders, mood disorders associated with premenstrual
syndrome, and postpartum depression; dysthemia; bipolar disorders; cyclothymia; chronic
fatigue syndrome; stress-induced headache; cancer; irritable bowel syndrome, Crohn's
disease; spastic colon; post operative ileus; ulcer; diarrhea; stress-induced fever; human
immunodeficiency virus infections; neurodegenerative diseases; gastrointestinal diseases;
eating disorder; hemorrhagic stress; chemical dependencies or addictions; drug or alcohol
withdrawal symptoms; stress-induced psychotic episodes; euthyroid sick syndrome;
syndrome of inappropriate antidiuretic hormone; obesity; infertility; head trauma; spinal cord
trauma; ischemic neuronal damage; excitotoxic neuronal damage; stroke; immune
dysfunctions; muscular spasms; urinary incontinence; senile dementia of the Alzheimer's

type; multi infarct dementia; amyotrophic lateral sclerosis; hypertension; tachycardia; congestive heart failure; osteoporosis; premature birth; hypoglycemia, and Syndrome X in a mammal or bird, comprising an amount of a compound according to claim 1 that is effective in the treatment of such disorder or condition, and a pharmaceutically acceptable carrier.

B² cont
Claim 14 (Twice Amended). A pharmaceutical composition according to claim 13 for the treatment of a disorder selected from inflammatory disorders; pain, asthma, psoriasis and allergies; generalized anxiety disorder; panic; phobias; obsessive compulsive disorder; post-traumatic stress disorder; sleep disorders induced by stress; pain perception; mood disorders; dysthemia; bipolar disorders; cyclothymia; fatigue syndrome; stress induced headache; cancer; irritable bowel syndrome, Crohn's disease; spastic colon; human immunodeficiency virus (HIV) infections; neurodegenerative diseases; gastrointestinal diseases; eating disorders; chemical dependencies and addictions; obesity; infertility; head traumas; spinal cord trauma; ischemic neuronal damage; excitotoxic neuronal damage; epilepsy; stroke; immune dysfunctions; muscular spasms; urinary incontinence; senile dementia of the Alzheimer's type; multi infarct dementia; amyotrophic lateral sclerosis; and hypoglycemia in a mammal.

B³
Claim 29 (Amended). A compound as claimed in claim 1 wherein R₂₄ and R₂₅ are selected from -CF₃, -CHF₂, CF₂CF₃, and CH₂CF₃,

B⁴
Claim 32 (Amended). A pharmaceutical composition as claimed in claim 14 for treatment of depression, selected from the group consisting of major depression, single episode depression, recurrent depression, and child abuse induced depression.

B⁵
Claim 36 (Amended). A pharmaceutical composition as claimed in claim 14 for treatment of stress induced immune dysfunctions selected from the group consisting of porcine stress syndrome, bovine shipping fever, equine paroxysmal fibrillation, confinement dysfunction in chicken, sheering stress in sheep, and human animal interaction stress in dogs.

B⁶
Claim 39 (Amended). A pharmaceutical composition as claimed in claim 44 for treatment of cerebral ischemia selected from cerebral hippocampal ischemia.

Claim 40 (Amended). A pharmaceutical composition as claimed in claim 14 for treatment of including social phobia, agoraphobia or specific phobias.

Please add the following claims:

Claim 41. The pharmaceutical composition according to claim 13 wherein the pain perception is fibromyalgia.

Claim 42. The pharmaceutical composition according to claim 13 wherein the ischemic neuronal damage is cerebral ischemia.

31 Claim 43. The pharmaceutical composition according to claim 14 wherein mood disorder is depression or postpartum depression.

Claim 44. The pharmaceutical composition according to claim 14 wherein the ischemic neuronal damage is cerebral ischemia.

Claim 45. The pharmaceutical composition according to claim 14 wherein the mammal is a human.
